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NEWS	4	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS	5	FEB 05	German (DE) application and patent publication number format changes
NEWS	6	MAR 03	MEDLINE and LMEDLINE reloaded
NEWS	7	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS	8	MAR 03	FRANCEPAT now available on STN
NEWS	9	MAR 29	Pharmaceutical Substances (PS) now available on STN
NEWS	10	MAR 29	WPIFV now available on STN
NEWS	11	MAR 29	New monthly current-awareness alert (SDI) frequency in RAPRA
NEWS	12	APR 26	PROMT: New display field available
NEWS	13	APR 26	IFIPAT/IFIUDB/IFICDB: New super search and display field available
NEWS	14	APR 26	LITALERT now available on STN
NEWS	15	APR 27	NLDB: New search and display fields available
NEWS	16	May 10	PROUSDDR now available on STN
NEWS	17	May 19	PROUSDDR: One FREE connect hour, per account, in both May and June 2004
NEWS	18	May 12	EXTEND option available in structure searching
NEWS	19	May 12	Polymer links for the POLYLINK command completed in REGISTRY
NEWS	20	May 17	FRFULL now available on STN
NEWS	21	May 27	STN User Update to be held June 7 and June 8 at the SLA 2004 Conference
NEWS	22	May 27	New UPM (Update Code Maximum) field for more efficient patent SDIs in CAplus
NEWS	23	May 27	CAplus super roles and document types searchable in REGISTRY
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NEWS WWW	CAS World Wide Web Site (general information)

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=> file medline biosis scisearch biotechno caplus
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=> s lymphotoxin
L1 11251 LYMPHOTOXIN

=> s l1 and p33
L2 16 L1 AND P33

=> s l1 and beta
L3 5595 L1 AND BETA

=> s lymphotoxin-beta
L4 1441 LYMPHOTOXIN-BETA

=> s l4 and p33
L5 0 L4 AND P33

=> s l4 and hiv
L6 15 L4 AND HIV

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7 9 DUP REM L6 (6 DUPLICATES REMOVED)

=> d ti 1-9

L7 ANSWER 1 OF 9 MEDLINE on STN DUPLICATE 1
TI Cytokine networks are pre-activated in T cells from **HIV**-infected patients on HAART and are under the control of cAMP.

L7 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
TI Apparatus and method for flow electroporation of biological samples

L7 ANSWER 3 OF 9 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
TI Antiviral mediated suppression of NF-kappaB and induction of the EBV lytic cycle; a novel therapy for EBV-associated Burkitt's lymphoma.

L7 ANSWER 4 OF 9 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
TI Microarray analysis of brains from macaques with lentiviral encephalopathy

showed up-regulation of genes that promote virus replication and down-regulation of neurotrophic genes.

L7 ANSWER 5 OF 9 MEDLINE on STN DUPLICATE 2
TI Signaling through the **lymphotoxin-beta** receptor stimulates **HIV**-1 replication alone and in cooperation with soluble or membrane-bound TNF-alpha.

L7 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
TI Soluble **lymphotoxin-beta** receptors, anti-lymphotoxin receptor antibodies, and anti-lymphotoxin ligand antibodies as therapeutic agents for the treatment of immunological diseases

L7 ANSWER 7 OF 9 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
TI Tumor necrosis factor receptor-associated factor (TRAF) 5 and TRAF2 are involved in CD30-mediated NF kappa B activation

L7 ANSWER 8 OF 9 MEDLINE on STN
TI TRAF5, an activator of NF-kappaB and putative signal transducer for the **lymphotoxin-beta** receptor.

L7 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
TI **Lymphotoxin-.beta.** and its therapeutic uses

=> d 9 8 5 ab

L7 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AB **Lymphotoxin-.beta.** (LT-β), a membrane protein of lymphocytes and a number of other cell types including phorbol ester (PMA) stimulated T cell hybridoma II-23.D7 cells, is isolated and characterized and a cDNA encoding it is cloned and expressed. **Lymphotoxin-.beta.** forms complexes with other peptides such as lymphotoxin-α (LT-α) and also forms homooligomers. The protein is involved targetting LT-α to the cell surface. The LT-α/LT-β complex may act as an inflammation regulating agent, a tumor growth inhibiting agent, a T cell inhibiting agent, a T cell activating agent, an autoimmune disease regulating agent, or an **HIV** inhibiting agent (no data). Furthermore, the antitumor activity of the LT-α/LT-β complex may be delivered to tumor cells by tumor infiltrating lymphocytes (TILs) transfected with the gene for LT-β (no data). LT-β was identified as the protein with which LT-α was bound on the surface of T-cells. The protein was only found in B- and T-cells. Cloning of a cDNA for LT-β by PCR using amino acid sequence-derived primers is described; the cDNA was expressed using the pCDM8 expression cassette with successful expression achieved even without the initiator AUG codon.

L7 ANSWER 8 OF 9 MEDLINE on STN
AB Tumor necrosis factor (TNF) receptor-associated factors (TRAFs) are signal transducers for several members of the TNF receptor superfamily. We have identified a novel member of the TRAF family by degenerate oligonucleotide polymerase chain reaction amplification that contains a zinc RING finger and zinc finger motifs, a coiled-coil region, and a C-terminal "TRAF" homology domain. In vitro translated TRAF5 binds to the cytoplasmic region of the **lymphotoxin-beta** receptor (LT-betaR) but not to several other related receptors including CD40, both TNF receptors, Fas, and nerve growth factor receptor. TRAF5 and LT-betaR coimmunoprecipitate when overexpressed in COS7 cells. TRAF5 mRNA expression is found in all visceral organs and overlaps with LT-betaR. These features distinguish TRAF5 from the other members of the TRAF family. The transcription factor NF-kappaB is activated in HEK293 cells by overexpression of full-length TRAF5 but not a truncated form lacking the zinc binding region. Furthermore, overexpression of LT-betaR in

HEK293 cells also results in activation of NF-kappaB, which is partially inhibited by the truncated TRAF5 mutant. These results show TRAF5 is functionally similar to TRAF2 in that both mediate activation NF-kappaB and implicate TRAF5 as a signal transducer for LT-betaR.

L7 ANSWER 5 OF 9 MEDLINE on STN DUPLICATE 2
AB The level of ongoing **HIV**-1 replication within an individual is critical to **HIV**-1 pathogenesis. Among host immune factors, the cytokine TNF-alpha has previously been shown to increase **HIV**-1 replication in various monocyte and T cell model systems. Here, we demonstrate that signaling through the TNF receptor family member, the **lymphotoxin-beta** (LT-beta) receptor (LT-betaR), also regulates **HIV**-1 replication. Furthermore, **HIV**-1 replication is cooperatively stimulated when the distinct LT-betaR and TNF receptor systems are simultaneously engaged by their specific ligands. Moreover, in a physiological coculture cellular assay system, we show that membrane-bound TNF-alpha and LT-alpha1beta2 act virtually identically to their soluble forms in the regulation of **HIV**-1 replication. Thus, cosignaling via the LT-beta and TNF-alpha receptors is probably involved in the modulation of **HIV**-1 replication and the subsequent determination of **HIV**-1 viral burden in monocytes. Intriguingly, surface expression of LT-alpha1beta2 is up-regulated on a T cell line acutely infected with **HIV**-1, suggesting a positive feedback loop between **HIV**-1 infection, LT-alpha1beta2 expression, and **HIV**-1 replication. Given the critical role that LT-alpha1beta2 plays in lymphoid architecture, we speculate that LT-alpha1beta2 may be involved in **HIV**-associated abnormalities of the lymphoid organs.

=> d 9

L7 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:603367 CAPLUS
DN 121:203367
TI **Lymphotoxin**-.**beta**. and its therapeutic uses
IN Browning, Jeffrey; Ware, Carl F.
PA Biogen, Inc., USA; University of California
SO PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9413808	A2	19940623	WO 1993-US11669	19931202
	WO 9413808	A3	19940804		
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2150249	AA	19940623	CA 1993-2150249	19931202
	AU 9460483	A1	19940704	AU 1994-60483	19931202
	AU 692146	B2	19980604		
	EP 672143	A1	19950920	EP 1994-907045	19931202
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 08507201	T2	19960806	JP 1993-514235	19931202
	US 5661004	A	19970826	US 1995-484272	19950607
	JP 2004135676	A2	20040513	JP 2003-383099	20031112
PRAI	US 1992-990304	A	19921204		
	US 1990-544862	B1	19900627		
	JP 1994-514235	A3	19931202		
	WO 1993-US11669	W	19931202		
	US 1994-222614	B1	19940401		

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=> d his

     (FILE 'HOME' ENTERED AT 10:32:01 ON 07 JUN 2004)

     FILE 'MEDLINE, BIOSIS, SCISEARCH, BIOTECHNO, CAPLUS' ENTERED AT 10:32:37
     ON 07 JUN 2004
L1         11251 S LYMPHOTOXIN
L2            16 S L1 AND P33
L3          5595 S L1 AND BETA
L4          1441 S LYMPHOTOXIN-BETA
L5             0 S L4 AND P33
L6            15 S L4 AND HIV
L7             9 DUP REM L6 (6 DUPLICATES REMOVED)

=> dup rem l2
PROCESSING COMPLETED FOR L2
L8             4 DUP REM L2 (12 DUPLICATES REMOVED)

=> d 1-4 ab

L8   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2004 ACS on STN
AB   The title complex is disclosed. These proteins are found on the surface
     of a number of cells, including phorbol ester-stimulated T-cell-hybridoma
     II-23.07 cells. The proteins and complexes are useful as antiinflammatory
     agents, T-cell activating agents, tumor growth-inhibiting agents, and
     enhancers of tumor infiltrating lymphocytes; they may also be used in the
     treatment of human immunodeficiency virus infection. Lymphotoxin
     and the associated p33 protein were purified from phorbol myristoyl
     acetate-stimulated II-23.07 cells. The amino-terminal sequence(s) for
     p33 is reported; the amino acid sequence of the membrane-associated
     lymphotoxin band exactly matched that described for secreted
     lymphotoxin. The functional relevance of total tumor necrosis
     factor or lymphotoxin to T-cell activation is described.

L8   ANSWER 2 OF 4     MEDLINE on STN                    DUPLICATE 1
AB   The expression of membrane-associated forms of lymphotoxin (LT)
     and TNF were examined on cell lines of T, B, and myeloid origin, IL-2
     dependent T cell clones, and peripheral blood lymphocytes. Inducible and
     constitutive patterns of surface LT expression were found on T cells as
     exemplified by the II-23.D7, a CD4+T cell hybridoma, and HUT-78, a T cell
     lymphoma. Phorbol ester induced surface LT expression on Ramos, an EBV
     transformed B cell line, but at a slower rate of appearance when compared
     to the II-23.D7. Secretion of LT was rapidly inducible by phorbol ester
     in II-23.D7 and also in HUT-78 but with slower kinetics; surface LT
     expression continued in both lines after secretion had ceased. Low levels
     of membrane TNF were transiently induced on II-23.D7 and HUT-78, but none
     was observed on Ramos. Peripheral blood monocytes and some myeloid tumor
     lines did not express surface LT. Several T cell clones expressed surface
     LT after Ag-specific stimulation, and expression persisted several days.
     Stimulation through the TCR or by IL-2 rapidly induced surface LT on
     resting peripheral T cells and CD56+ NK cells; pokeweed mitogen activation
     induced expression on CD20+ B cells. Consistent with previous results,
     immunoprecipitation with anti-LT mAb showed that LT was complexed with a
     distinct 33 kDa glycoprotein (p33) on cells that expressed
     surface LT, whereas secreted LT was not associated with p33.
     Surface and secreted modes of LT expression by activated T, B, and NK
     cells suggests that LT can be utilized as either a localized or diffusible
     mediator in immune responses.

L8   ANSWER 3 OF 4     MEDLINE on STN                    DUPLICATE 2
AB   We characterized the membrane-associated form of lymphotoxin
     (surface LT) on the activated II-23.D7 T cell hybridoma. Antibodies to
     rLT precipitated both surface LT and a distinct 33-kDa glycoprotein (
     p33). Because p33 and surface LT were antigenically
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unrelated, their coprecipitation suggested a physical association of **p33** and surface LT on the membrane. Pulse-chase analysis indicated that LT and **p33** associate with each other early in the LT biosynthetic pathway, precluding the possibility that LT is secreted and bound to **p33** or a surface receptor. Furthermore, no **p33** was associated with the secreted form of LT. Isoelectric focusing of surface LT and **p33** under nondenaturing and denaturing conditions confirmed that surface LT and **p33** existed as a complex. Treatment of cells with a high concentration of salt or with acid indicated that surface LT is a peripheral membrane protein. Although secreted LT is a homologous trimer, protein cross-linking studies revealed that surface LT existed as a monomer associated with a dimer of **p33**. Together the results demonstrate a novel mechanism for stable membrane expression of LT by activated T cells.

L8 ANSWER 4 OF 4 MEDLINE on STN DUPLICATE 3

AB A human T cell hybridoma, II-23.D7, was induced with phorbol ester to express a surface form of **lymphotoxin** (LT, TNF-beta) and an associated 33-kDa glycoprotein. The LT epitopes were detected by surface immunofluorescence staining and by immunoprecipitation from radioiodinated or biosynthetically labeled cells with the use of anti-rLT polyclonal and monoclonal antibodies. The epitopes detected by the antibody were related to LT because adsorption of the anti-rLT with PMA-activated II-23.D7 cells resulted in the removal of the neutralizing titer of the anti-rLT antiserum. Immunoprecipitation of surface radioiodinated II-23.D7 cells revealed two bands of 25 kDa and 33 kDa that were specifically precipitated with anti-rLT, but not anti-rTNF antibodies. Enzymatic digestion with glycanases showed both proteins to have N-linked carbohydrate, with O-linked sugar limited to the 25-kDa protein. To determine the biochemical relationship between these proteins, the two LT-like forms were purified from detergent-solubilized II-23.D7 cells by immunoaffinity chromatography. Peptide mapping using CNBr cleavage showed the 25-kDa surface form to be identical to rLT, whereas the 33-kDa protein was different. Biosynthetic labeling studies showed that **p33** contained both methionine and cysteine, whereas the p25 contained only methionine. Thus, the surface LT form lacks a leader peptide indicating an anchoring mechanism distinct from that described for membrane TNF. The nature of the attachment of this LT form to the membrane surface is not clear, however, neither TNF receptor binding nor lipid linkages appear to be involved. The accessory protein, **p33**, may anchor LT to the surface. These findings identify a new characteristic of LT and point toward an additional pathway by which T lymphocytes may mediate cytolytic activity and regulate inflammatory processes.

=> d 2

L8 ANSWER 2 OF 4 MEDLINE on STN DUPLICATE 1

AN 93094581 MEDLINE

DN PubMed ID: 1281193

TI Expression of surface **lymphotoxin** and tumor necrosis factor on activated T, B, and natural killer cells.

AU Ware C F; Crowe P D; Grayson M H; Androlewicz M J; Browning J L

CS Division of Biomedical Sciences, University of California, Riverside 92521-0121.

NC DK-07310 (NIDDK)

SO Journal of immunology (Baltimore, Md. : 1950), (1992 Dec 15) 149 (12) 3881-8.
Journal code: 2985117R. ISSN: 0022-1767.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 199301

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ED   Entered STN: 19930129
     Last Updated on STN: 19960129
     Entered Medline: 19930114


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     FILE 'MEDLINE, BIOSIS, SCISEARCH, BIOTECHNO, CAPLUS' ENTERED AT 10:32:37
     ON 07 JUN 2004
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L5             0 S L4 AND P33
L6            15 S L4 AND HIV
L7             9 DUP REM L6 (6 DUPLICATES REMOVED)
L8             4 DUP REM L2 (12 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 10:42:27 ON 07 JUN 2004

=> s l4 and immun?
               0 LYMPHOTOXIN
               0 BETA
               0 LYMPHOTOXIN-BETA
                   (LYMPHOTOXIN(W)BETA)
              15 IMMUN?
L9             0 L4 AND IMMUN?

=> s l4 and neoplasm
               0 LYMPHOTOXIN
               0 BETA
               0 LYMPHOTOXIN-BETA
                   (LYMPHOTOXIN(W)BETA)
               0 NEOPLASM
L10            0 L4 AND NEOPLASM

=> s l4 and lupus
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               0 BETA
               0 LYMPHOTOXIN-BETA
                   (LYMPHOTOXIN(W)BETA)
               0 LUPUS
L11            0 L4 AND LUPUS

=> s l4 and diabetes
```

	0	LYMPHOTOXIN
	0	BETA
	0	LYMPHOTOXIN-BETA (LYMPHOTOXIN(W)BETA)
	1	DIABETES
L12	0	L4 AND DIABETES

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DATE: Monday, June 07, 2004

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☐	L7	l4 or l5	14
☐	L6	l4 or l5L5	17
☐	L5	p33 and l2	7
☐	L4	p33 and L3	14
☐	L3	L1 and immun$	1178
☐	L2	L1 and neoplasia	118
☐	L1	lymphotoxin	1205

END OF SEARCH HISTORY